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Remarks

Restriction requirement

Claims 1-63 were restricted into three groups of claims. The applicants elect Group III claims with traverse.

Group I claims include claims 1-25 and 62-63 which are drawn to a nucleic acid fragment encoding polyhydroxyalkanoic acid (PHA) synthase and a fatty acid-acyl-coenzyme A transferase. Group II claims include claims 26-38 which are drawn to a method of transforming a cell using the nucleic acid fragment. Group III claims include claims 38-61 which are drawn to a method of producing polyester using the transformed cell.

Claims 1-25 and 62-63 are drawn to a **single** fragment of nucleic acid . The critical aspect of claims 1-25 and 62-63 is the co-expression of (1) a PHA synthase and (2) a fatty acid:acyl-CoA transferase in a **single nucleic acid construct**. This is the inventive feature which links the subject matter in the three groups of claims.

The cited reference, U.S. Patent No. 6,117,658 to Dennis et al. ("Dennis"), disclose a cell which has genes expressing the PHA biosynthetic pathway and genes expressing the succinyl-

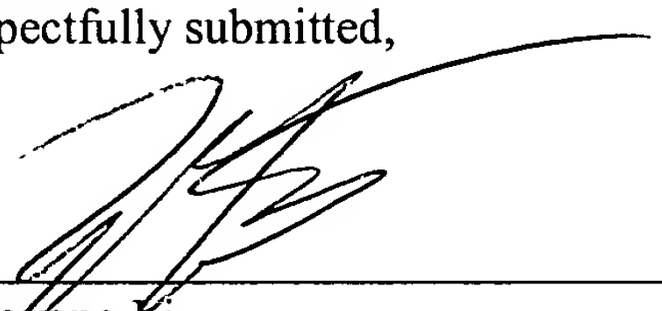
CoA metabolic pathway, the genes expressing the succinyl-CoA including a 4-hydroxybutyrate acyl-CoA transferase (col. 6, lines 59-67; col. 8, line 48 to col. 9, line 39). However, there is no disclosure in Dennis of a **single** nucleic acid fragment which expresses **both** a PHA synthase **and** a fatty acid acyl-CoA transferase. Therefore, Dennis does not anticipate claims 1-63.

Neither does Dennis make obvious claims 1-63. Dennis does not provide one of ordinary skill in the art a motivation to modify Dennis to arrive at the claimed subject matter which requires **both** a PHA synthase **and** a fatty acid acyl-CoA transferase to be expressed in a **single** nucleic acid fragment. Even if Dennis provided such a motivation, one of ordinary skill in the art still will not have a reasonable expectation of success of the co-expression of a PHA synthase and a fatty acid acyl-CoA transferase alone, not the whole succinic semialdehyde metabolic pathway as required in Dennis (col. 5, line 66 to col. 6, line 3), in a single nucleic acid fragment for the production of PHAs having 4-hydroxyalkanoate monomer units. Therefore, Dennis does not render claims 1-63 prima facie obvious under 35 U.S.C. § 103.

Even if one argued that Dennis rendered claims 1-63 prima facie obvious, the superior results obtained in the present application over Dennis would rebut any prima facie obviousness, if any. For example, Dennis was only able to produce PHAs having very low content of 4HB (0 to 1.5 mol%, col. 24, lines 10 to 19, Table 1; 5 mol%, col. 26, lines 5-7). In sharp contrast, the applicants were able to produce PHAs having 4HB content ranging from 28% to 100% (p. 23, Table 1 and p. 25, Table 2). Therefore, claims 1-63 are inventive over Dennis.

Withdrawal of the restriction requirement and allowance of claims 1-63 are earnestly solicited. A copy of the claims as pending is attached in the Appendix for the Examiner's convenience.

Respectfully submitted,



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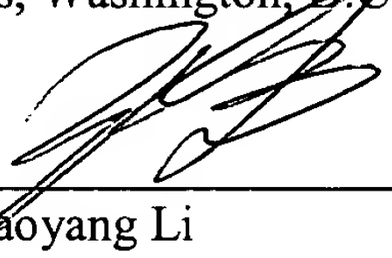
CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)

I hereby certify that this RESPONSE TO RESTRICTION REQUIREMENT, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231.



Zhaoyang Li

Date: September 13, 2001

Appendix I. Claims as pending

1. A nucleic acid segment encoding:

   a) a polyhydroxyalkanoic acid synthase protein; and

   b) a fatty acid:acyl-CoA transferase protein.

2. The nucleic acid segment of claim 1, wherein the polyhydroxyalkanoic acid synthase protein is an *Alcaligens entrophus* polyhydroxyalkanoic acid synthase protein.

3. The nucleic acid segment of claim 2, wherein the *Alcaligenes eutrophus* polyhydroxyalkanoic acid synthase protein is encoded by the *Alcaligenes eutrophus phaC* polyhydroxyalkanoic acid synthase structural gene.

4. The nucleic acid segment of claim 1, wherein the fatty acid:acyl-coenzyme A transferase protein is a 4-hydroxybutyrate:acyl-CoA transferase protein.

5. The nucleic acid segment of claim 4, wherein the 4-hydroxybutyrate:acyl-coenzyme A transferase protein is a *Clostridium kluyveri* 4-hydroxybutyrate:acyl-coenzyme A transferase protein.

6. The nucleic acid segment of claim 5, wherein the 4-hydroxybutyrate:acyl-coenzyme A transferase protein is encoded by the *Clostridium kluyveri orfZ* 4-hydroxybutyrate:acyl-coenzyme A transferase structural gene.

7. The nucleic acid segment of claim 1, further comprising a promoter functional in bacterial cells.

8. The nucleic acid segment of claim 1, wherein:

a) The sequence encoding a polyhydroxyalkanoic acid synthase protein is operably linked to its native promoter; and

b) the sequence encoding a fatty acid:acyl-coenzyme A transferase protein is operably linked to its native promoter.

9. The nucleic acid segment of claim 1, further comprising a promoter heterologous to:

a) the sequence encoding a polyhydroxyalkanoic acid synthase protein; and

b) the sequence encoding a fatty acid:acyl-coenzyme A transferase protein.

10. A recombinant vector comprising the nucleic acid segment of claim 1.

11. A recombinant vector comprising the nucleic acid segment of claim 9.

12. The recombinant vector of claim 11, further defined as vector pKSSE.3.

13. The recombinant vector of claim 11, further defined as vector pSKSE.3.

14. A recombinant vector comprising:

a) nucleic acid segment encoding a polyhydroxyalkanoic acid synthase protein;

b) a nucleic acid segment encoding a fatty acid:acyl-coenzyme A transferase protein; and

c) a promoter heterologous to the nucleic acid segment encoding a polyhydroxyalkanoic acid synthase protein, and heterologous to the nucleic acid segment encoding a fatty acid:acyl-coenzyme A transferase protein.

15. A cell comprising a nucleic acid segment, the nucleic acid segment encoding:

a) a polyhydroxyalkanoic acid synthase protein; and

b) a fatty acid:acyl-coenzyme A transferase protein.

16. The cell of claim 15, further defined as a plant cell, mammalian cell, insect cell, fungal cell, or bacterial cell.

17. The cell of claim 16, wherein the cell is a plant cell.

18. The cell of claim 16, wherein the cell is a bacterial cell.

19. The bacterial cell of claim 18, wherein the bacterial cell is *Escherichia coli*.

20. The bacterial cell of claim 19, wherein the bacterial cell is strain *Escherichia coli* XL1-Blue.

21. The cell of claim 15, wherein the polyhydroxyalkanoic acid synthase protein is a *Alcaligenes eutrophus* polyhydroxyalkanoic acid synthase protein.

22. The cell of claim 21, wherein the *Alcaligenes eutrophus* polyhydroxyalkanoic acid synthase protein is encoded by the *Alcaligenes eutrophus phaC* polyhydroxyalkanoic acid synthase structural gene.

23. The cell of claim 15, wherein the fatty acid:acyl-coenzyme A transferase protein is a 4-hydroxybutyrate:acyl-coenzyme A transferase protein.

24. The cell of claim 23, wherein the 4-hydroxybutyrate:acyl-coenzyme A transferase protein is a *Clostridium kluyveri* 4-hydroxybutyrate:acyl-coenzyme A transferase protein.

25. The cell of claim 24, wherein the *Clostridium kluyveri* 4-hydroxybutyrate:acyl-coenzyme A transferase protein is encoded by the *Clostridium kluyveri orfZ* 4-hydroxybutyrate:acyl-coenzyme A transferase structural gene.

26. A method for preparing a transformed cell, comprising the steps:

a) selecting a host cell;

b) contacting the host cell and a nucleic acid segment, the nucleic acid segment encoding:

i) a polyhydroxyalkanoic acid synthase protein; and

ii) a fatty acid:acyl-coenzyme A transferase protein

under conditions suitable for uptake of the nucleic acid segment by the host cell; and

c) regenerating the cell to produce a transformed cell.

27. The method of claim 26, wherein the contacting step is further defined as calcium chloride mediated transformation.

28. The method of claim 26, wherein the cell is a plant cell, mammalian cell, insect cell, fungal cell, or bacterial cell.

29. The method of claim 28, wherein the cell is a plant cell.

30. The method of claim 28, wherein the cell is a bacterial cell.

31. The method of claim 30, wherein the bacterial cell is *Escherichia coli*.

32. The method claim 31, wherein the bacterial cell is *Escherichia coli* strain XL1-Blue.

33. The method of claim 26, wherein the polyhydroxyalkanoic acid synthase protein is an *Alcaligenes eutrophus* polyhydroxyalkanoic acid synthase protein.

34. The method of claim 33, wherein the *Alcaligenes eutrophus* polyhydroxyalkanoic acid synthase protein is encoded by the *Alcaligenes eutrophus phaC* polyhydroxyalkanoic acid synthase structural gene.

35. The method of claim 26, wherein the fatty acid:acyl-coenzyme A transferase protein is a 4-hydroxybutyrate:acyl-coenzyme A transferase protein.

36. The method of claim 35, wherein the 4-hydroxybutyrate:acyl-coenzyme A transferase protein is a *Clostridium kluyveri* 4-hydroxybutyrate:acyl-coenzyme A transferase protein.

37. The method of claim 36, wherein the *Clostridium kluyveri* 4-hydroxybutyrate:acyl-coenzyme A transferase protein is encoded by the *Clostridium kluyveri orfZ* 4-hydroxybutyrate:acyl-coenzyme A transferase structural gene.

38. A method for the preparation of a polyester, comprising the steps of:

a) obtaining a cell capable of producing:

i) a polyhydroxyalkanoic acid synthase protein; and

ii) a fatty acid:acyl-coenzyme A transferase protein;

b) establishing a culture of the cell;

c) culturing the cell under conditions suitable for the production of the polyester; and

d) isolating the polyester from the cell.

39. The method of claim 38, wherein the cell is a plant cell, mammalian cell, insect cell, fungal cell, or bacterial cell.

40. The method of claim 39, wherein the cell is a plant cell.

41. The method of claim 39, wherein the cell is a bacterial cell.

42. The method of claim 41, wherein the cell is *Escherichia coli*.

43. The method of claim 42, wherein the bacterial cell is *Eschrichia coli* strain XL1-Blue.

44. The method of claim 38, wherein the polyhydroxyalkanoic acid synthase protein is a polyhydroxyalkanoic acid synthase protein from *Alcaligenes eutrophus*.

45. The method of claim 44, wherein the *Alcaligenes eutrophus* polyhydroxyalkanoic acid synthase protein is encoded by the *Alcaligenes eutrophus* polyhydroxyalkanoic acid synthase structural gene.

46. The method of claim 38, wherein the fatty acid:acyl-coenzyme A transferase protein is a 4-hydroxybutyrat:acyl-coenzyme A transferase protein.

47. The method of claim 46, wherein the 4-hydroxybutyrate:acyl-coenzyme A transferase protein is a *Clostridium kluyveri* 4-hydroxybutyrate:acyl-coenzyme A transferase protein.

48. The method of claim 47, wherein the *Clostridium kluyveri* 4-hydroxybutyrate:acyl-coenzyme A transferase protein is encoded by *Clostridium kluyveri orfZ* 4-hydroxybutyrate:acyl-coenzyme A transferase structural gene.

49. The method of claim 38, wherein the culture contains glucose.

50. The method of claim 38, wherein the culture contains 4-hydroxybutyric acid, the sodium salt of 4-hydroxybutyric aicd, γ-butyrolactone, 1,4-butanediol, 4-hydroxyvaleric acid, γ-valerolactone, 1,4-pentanediol, 3-hydroxybutyric acid, the sodium salt of 3-hydroxybutyric acid, a hydroxypropionic acid, a hydroxybutyric acid, a hydroxyvaleric acid, a hydroxycaproic acid, a hyroxyheptanoic acid, a hydroxyoctanoic acid, a hydroxydecanoic acid, γ-caprolactone, γ-heptanolactone, γ-octanolactone, or γ-decanolactone.

51. The method of claim 38, wherein the culture contains molecular oxygen.

52. The method of claim 38, wherein the cell is further capable of producing a protein capable of hydrolysing a lactone to the corresponding hydroxyalkanoic acid.

53. The method of claim 38, wherein the cell is further capable of producing a 2-oxyglutarate decarboxylase protein and a 4-hydroxybutyrate dehydrogenase protein.

54. The method of claim 38, wherein the cell is further capable of producing a succinate;acetyl-Coenzyme A trasferase protein, a succiniate-semialdehyde dehydrogenase protein, and a 4-hydroxybutyrate dehydrogenase protein.

55. The method of claim 38, wherein the cell is further capable of producing a succinate-semialdehyde dehydrogenase protein, and a 4-hydroxybutyrate dehydrogenase protein.

56. The method of claim 38, wherein the cell is further capable of producing a 2-methylcitrate synthase protein, a 2-methylcitrate dehydratase protein, a 2-methylisocitrate dehydratase protein, a 2-methylisocitrate lyase protein, a succinate:acetyl-Coenzyme A transferase protein, a succinate-semialdehyde dehydrogenase protein, and a 4-hydroxybutyrate dehydrogenase protein.

57. The method of claim 38, wherein the polyester is a homopolyester.

58. The method of claim 57, wehrein the homopolyester is poly(4-hydroxybutyric acid).

59. The method of claim 57, wherein the homopolyester is poly(3-hydroxybutyric acid).

60. The method of claim 38, wherein the polyester is a copolyester.

61. The method of claim 60, wherein the copolyester is poly(3-hydroxybutyric acid –co-4-hydroxybutyric acid).

62. The nucleic acid segment of claim 1, wherein the polyhydroxyalkanoic acid synthase protein is encoded by a sequence comprising SEQ ID NO: 1.

63. The nucleic acid segment of claim 1, wherein the fatty acid:acyl-CoA transferase protein is encoded by a sequence comprising SEQ ID NO: 2.